REMARKS

Claims 1, 2, 4-6, and 43-46 are pending in the application. Claims 1, 2, 4-6, and 43-46 stand rejected. Claims 1 and 4 have been amended. Reconsideration and allowance of Claims 1, 2, 4-6, and 43-46 is respectfully requested.

The Objection to Claims 4-6

Claim 4 has been amended to recite "restriction fragment length polymorphism analysis" as suggested by the Examiner. Removal of the objection to Claims 4-6 is respectfully requested.

The Rejection of Claims 1-2, 4-6, and 43-46 Under 35 U.S.C. § 112, Second Paragraph

Claims 1-2, 4-6, and 43-46 stand rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. In particular, the Examiner has taken the position that Claims 1-2, 4-6, and 43-46 are indefinite because it is unclear how the recitation of SEQ ID NO:3 limits the claims. While not acquiescing with the Examiner's position, but in order to facilitate prosecution, Claim 1, from which Claims 2, 4-6, and 43-46 depend, has been amended to recite "[a] method for identifying a genetic mutation that is associated with adult onset cerebellar ataxia in a human subject.. (b) comparing the first nucleic acid sequence to SEQ ID NO:3 to identify a difference between the first nucleic acid sequence from the first human subject exhibiting adult onset cerebellar ataxia and SEQ ID NO:3 ...." Support for this amendment is found in the specification as filed, for example at page 11, lines 11-25.

Accordingly, removal of this ground of rejection is respectfully requested.

The Rejection of Claims 1-2, 4-6, and 43-46 Under 35 U.S.C. § 112, First Paragraph (Enablement)

Claims 1-2, 4-6, and 43-46 stand rejected under 35 U.S.C. § 112, first paragraph, for lack of enablement. The Examiner has acknowledged that the specification is enabling for methods

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comprising identifying the H101Y and/or S119P PKC gamma gene mutations in a human subject and confirming these mutations as being associated with adult onset cerebellar ataxia in a human subject. However, the Examiner has taken the position that the specification does not reasonably provide enablement for methods comprising identifying and confirming any other PKC gamma gene mutations as being associated with adult onset cerebellar ataxia. The Examiner asserts that it is unpredictable as to whether one of skill in the art could use applicants' invention in a manner commensurate with the instant claims, and that it would require undue experimentation to use applicants' invention as it is broadly claimed. Applicants respectfully disagree with the Examiner's conclusion for at least the following reasons.

While not acquiescing with the Examiner's position, but in order to facilitate prosecution, Claim 1 has been amended to remove the phrase "comprising determining that the identified nucleic acid sequence difference is also present in a plurality of human subjects exhibiting adult onset cerebellar ataxia and is absent in a plurality of human subjects not exhibiting adult onset cerebellar ataxia." As amended, Claim 1 recites as follows:

> A method of identifying a genetic mutation that is associated with adult onset cerebellar ataxia in a human subject, said method comprising:
>
> (a) determining a first nucleic acid sequence of a human protein kinase C gamma gene from a first human subject exhibiting adult onset cerebellar ataxia;
>
> (b) comparing the first nucleic acid sequence to SEQ ID NO:3 to identify a difference between the first nucleic acid sequence from the first human subject exhibiting adult onset cerebellar ataxia and SEQ ID NO:3, wherein the difference alters the amino acid sequence encoded by the human protein kinase C gamma gene; and

(c) confirming that the difference identified between the first nucleic acid sequence and SEQ ID NO:3 is a genetic mutation associated with adult onset cerebellar ataxia by co-segregation analysis.

It is submitted that Claims 1-2, 4-6, and 43-46 are enabled by the specification as filed in view of the knowledge of the skilled artisan at the time the application was filed. The Examiner has acknowledged that the specification is enabling for methods comprising identifying the H101Y and/or S119P PKC gamma gene mutations in a human subject and confirming these mutations as being associated with adult onset cerebellar ataxia in a human subject. However, the Examiner has taken the view that one of skill in the art would require the establishment of an association that is significant based on statistical analysis for concluding that a particular mutation is disease associated. In this regard, it is noted that the specification defines the term 'genetic mutation' recited in Claim 1 step (c) as an alteration of the wild-type protein kinase C gamma (PRKCG) sequence deposited in GENBANK, provided as SEQ ID NO:3 that is not a recognized polymorphism (i.e., has a population frequency less than 1% in mammalian control subjects of the same species that do not exhibit ataxia). See specification at page 5, lines 1-4.

As previously described by applicants, adequate guidance is provided in the specification which allows for one of skill in the art to identify additional mutations associated with adult onset cerebellar ataxia through routine experimentation. See applicants' response to non-final Office Action mailed on June 15, 2007; Amendment After Final mailed on June 2, 2008; and Amendment Submitted With RCE mailed on July 29, 2008. As previously acknowledged by the Examiner, the skill level in the relevant art is high. As previously stated by the Examiner, "given the high level of skill of one skilled in the art relevant to the claimed invention, it is clearly within the ability of such an artisan to conduct screening methods, e.g. employing samples from other types of mammals and/or patients with other types of ataxia so as to determine whether

other mutations associated with ataxia exist in the protein kinase C gene of such subjects." See page 5 of non-final Office Action mailed February 15, 2007.

Moreover, as previously pointed out by applicants, the nature of experimentation required to practice the claimed invention is routine in the art, and not undue. In support of applicants' position regarding the routine nature of the experimentation required, applicants previously provided objective evidence that additional mutations in the protein kinase C gamma gene (SEQ ID NO:3) that co-segregate with ataxia have been successfully identified by others in the field. See Nolte, D., et al., *Movement Disorders 22*(2):265-267 (2007), provided as Attachment A in the response filed by applicants on June 15, 2007, describing the identification of the mutation G63V in two human subjects exhibiting ataxia which was not detected in control chromosomes from 200 healthy subjects. In addition, as summarized in TABLE 1 of Nolte et al., numerous other mutations that co-segregate with ataxia have been identified by others in the field after the priority date of the instant invention.

Therefore, it is demonstrated that only routine experimentation is required to practice the method of the invention in view of the guidance in the specification and the knowledge of those skilled in the art. Applicants respectfully request removal of this ground of rejection.

The Rejection of Claims 1-2, 4-6 and 43-46 Under 35 U.S.C.§ 102(a)

The Examiner has rejected Claims 1-2, 4-6, and 43-46 under 35 U.S.C.§ 102(a) as being anticipated by Chen et al., *Am. J. Hum. Genet. 72*:839-849 (April 2003).

Applicants respectfully point out that Chen et al. is disqualified as a citable prior art reference under 35 U.S.C. § 102(a) because the cited reference describes the inventors own work as set forth in the Declaration of inventor Dr. Wendy H. Raskind under 37 C.F.R. § 1.132 (hereafter "the Raskind Declaration"), submitted herewith as Attachment A. Accordingly, removal of this ground of rejection is respectfully requested.

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CONCLUSION

In view of the foregoing remarks, applicants submit that all of the pending claims are in condition for allowance and notification to this effect is respectfully requested.

Respectfully submitted,

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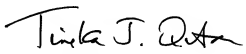

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